PREVENTIVE MEDICINE 13, 656–669 (1984)

The Influence of Passive Smoking on Pulmonary Function—A Study of 1,351 Office Workers[1]

MICHAEL KENTNER,[2] GERHARD TRIEBIG, AND DIETER WELTLE

Institute of Occupational and Social Medicine and Polyclinic of Occupational Diseases of the University of Erlangen–Nuremberg, Schillerstrasse 25/29, D-8520 Erlangen, Federal Republic of Germany

Until now it has been difficult to ascertain how much passive inhalation of tobacco smoke affects bronchopulmonary function. To answer this question, an investigation involving 1,351 white collar workers was carried out. Information about active and passive tobacco smoke exposure was obtained by a standardized questionnaire. This made it possible to subdivide the overall group into five subgroups: Never smokers, passive smokers, ex-smokers, current smokers, and other smokers. Forced expiratory vital capacity (FVC) and maximal expiratory flow-volume (MEFV) curves were used for lung function analysis. From these curves FVC, forced mid-expiratory flow (FEF 25/75), forced end-expiratory flow (FEF 75/85), and maximal mid-expiratory flow (MEF 25/75) were determined and standardized for sex, age, height, and body weight. Passive smokers evaluated by this method showed essentially no decrease in parameters describing ventilatory function. It is concluded from the dose- and time-effect relationships obtained in active smokers between the lung function parameters and the duration of tobacco smoke exposure on the one hand and the daily consumption of cigarettes on the other that passive smoking in small doses may have no essential effect on pulmonary function. © 1984 Academic Press, Inc.

INTRODUCTION

One of the numerous questions that have not yet been unequivocally answered with respect to passive smoking is its effect on bronchopulmonary function in people with healthy lungs. A number of studies in children indicate a certain negative influence, particularly in children of preschool age (11, 30, 33). Other studies, however, fail to confirm such an association (5, 18, 27, 29). Recent reviews on this subject can be found in publications by Weiss *et al.* (34) and by Lebowitz (19).

To date, only a few studies have been published on the effects of passive smoking and pulmonary function in adults (7, 14, 27, 35). These investigations were usually initiated within the framework of research projects not primarily concerned with passive smoking. As a result, certain restrictions must inevitably be made regarding the relevance of these findings. This point will be considered in more detail in the discussion. The investigation reported herein, in contrast, was designed and carried out for the sole purpose of confirming or denying any significant effects of passive smoking on the bronchopulmonary system using pulmonary function measurement.

[1] Presented at the Symposium "Medical Perspectives on Passive Smoking," April 9–12, 1984, Vienna, Austria.

[2] To whom reprint requests should be addressed.

0091-7435/84 $3.00
Copyright © 1984 by Academic Press, Inc.
All rights of reproduction in any form reserved.

2023383212

Source: https://www.industrydocuments.ucsf.edu/docs/nryx0000

PATIENTS AND METHODS

A total of 1,351 people (941 men and 410 women) took part in the study, which was carried out in 1982–1983. Participation in the study was voluntary. All participants were white-collar workers, the majority of whom were employed in sedentary office jobs. Test subjects were recruited from the staff of an administration authority and two large industrial companies located in Northern Bavaria, a region with a relatively low level of air pollution. All those participating anonymously filled out a standardized questionnaire specially developed for this study, and upon completion handed it in a closed envelope to the person carrying out the examinations.

The pulmonary function tests were carried out with an electronic spirometer.[3] The device was calibrated either daily or prior to each new series of measurements. The spirometric examination was conducted by two trained examiners with a knowledge of medicine. Special attention was paid to good cooperation on the part of the test subject with respect to the respiration exercises, which were generally repeated two to three times.

Of the various pulmonary function parameters, those listed in Table 1 were included in the further analysis. These parameters were identical to those used in comparable studies.

These data were transferred, anonymously, to documents designed for electronic data processing. Evaluation of the data was effected on a data processing system of the type Cyber 845.[4] After various plausibility checks and appropriate adjustment of the data record and group, the overall group was subdivided into five subgroups (Fig. 1):

(a) *Never smokers* (*NS*), defined as persons who have never been regularly exposed to tobacco smoke, either actively or passively.

(b) *Passive smokers* (*PS*), defined as subjects who have never actively smoked, but who are currently exposed to passive smoking. Here, three subgroups were differentiated:

(i) PS exclusively with household exposure to passive smoking (PS/H),
(ii) PS exposed passively to tobacco smoke only at their place of work (PS/W), and
(iii) persons with a combination of passive smoke exposure (PS/HW).

(c) *Ex-smokers* (*ES*), defined as persons who had given up active tobacco smoking at least 6 months previously.

(d) *Current smokers* (*CS*), representing the group of persons who, at the time of the investigation were actively smoking and inhaling the smoke.

(e) *Other smokers* (*OS*), representing a remaining category in which noninhaling cigarette smokers and cigar and pipe smokers were grouped together.

Considerable care was expended on the standardization of the analytical pulmonary function data. For all the pulmonary function parameters, on the basis of the NS group, formulae for internal predicted values were computed, using

[3] Siregnost FD10, XY Recorder E2218, Siemens, Erlangen, FRG.
[4] Control Data Corporation, Minneapolis, Minn.

2023383718

Source: https://www.industrydocuments.ucsf.edu/docs/nryx0000

TABLE 1
THE PARAMETERS EMPLOYED FOR PULMONARY FUNCTION ANALYSIS

Method	Pulmonary function parameter	Abbreviation
Forced vital capacity curve	Forced expiratory vital capacity	FVC
	Forced mid-expiratory flow	FEF 25/75
	Forced end-expiratory flow	FEF 75/85
Maximal expiratory flow–volume curve	Maximal mid-expiratory flow	MEF 25/75

multiple regression analyses, and taking into account sex, age, height, and body weight. A comparison of the reference values thus obtained, with standard values established by other authors (4, 17, 23, 26) shows a good level of agreement. According to these figures, the standard values decrease with increasing age and weight, while an increase in height results in an elevation in the predicted value (Table 2). All the individual values actually measured were converted into a percentage deviation from the predicted standard value.

The differences in the pulmonary function parameters standardized in this way were statistically checked in a subgroup comparison, using a nonparametric test procedure. This procedure involved a comparison of several independent samples as described by Kruskal and Wallis (36). A significance level of $P \leq 0.05$ was chosen.

RESULTS

Group Structure

Table 3 shows the size, average age, and prevalence of pulmonary disease in

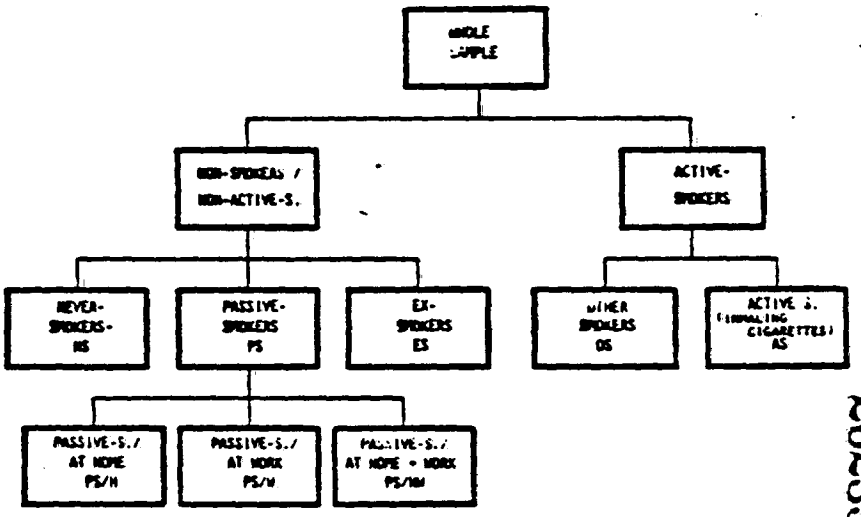

FIG. 1. Subgroups in accordance with tobacco smoke exposure criteria.

2023383719

TABLE 2
CORRECTION FACTORS FOR THE STANDARDIZATION OF THE PULMONARY FUNCTION PARAMETERS

		Age (years)	Height (m)	Weight (kg)	Const.
FVC	M	−0.028	5.71	−0.011	−3.37
(L)	F	−0.038	4.87	−0.003	−2.94
PEF 25/75	M	−0.020	4.30	−0.014	−1.72
(L/S)	F	−0.043	1.37	−0.020	1.27
PEF 75/85	M	−0.027	13.85	−0.048	−12.01
(L/S)	F	−0.091	6.48	−0.018	−0.36
MEF 25/75	M	−0.006	3.51	−0.029	−0.03
(L/S)	F	−0.023	1.84	0.031	0.03

each subgroup. The average age varies between 39 and 43 years for the men, and between 29 and 41 years for the women. Since almost all the pulmonary function parameters correlated negatively with age, the need for a standardization was thus underscored.

The CS group was most frequently affected by bronchopulmonary prior diseases, but the differences were not significant when compared with the other groups. Since on the one hand, passive inhalation of tobacco smoke may induce, or at least aggravate, chronic bronchitis, while active smoking may be the cause of this disease, the analysis of pulmonary function parameters would be affected by both including or excluding bronchitic subjects. It was, however, found that this had essentially no influence on the median values or the regression analysis. For this reason, a basic group, excluding subjects with bronchopulmonary diseases such as pneumonia, asthma, and tuberculosis in their history, but including the bronchitics, was used for further evaluation.

TABLE 3
STRUCTURE OF THE GROUP INTO SUBGROUPS. NUMBER OF SUBJECTS, AVERAGE AGE, AND BRONCHOPULMONARY PRIOR DISEASES

	No. of subjects examined		Age (median values)		Pneumonia, bronchial asthma, tuberc. of the lungs		Chronic bronchitis	
	M	F	M	F	M	F	M	F
NS	142	66	42	41	21	7	3	2
PS	251	132	40	36	30	17	8	3
ES	301	99	43	39	42	8	9	3
OS	64	12	41	29	5	2	1	2
CS	183	141	39	31	28	11	9	6
Su.	941	410	41	35	136	45	30	18

2023383720

Source: https://www.industrydocuments.ucsf.edu/docs/nryx0000

Pulmonary Function Parameters in a Comparison of the Subgroups

In the case of FVC (Fig. 2), the median values for men are similar in all five subgroups, while, in women, only that of the CS group differs significantly from the three groups of nonsmokers.

The comparison of FEF 25/75 (Fig. 3) values shows results similar to those seen for FVC, as do the results of FEV_1, not shown here. The greatest negative deviation of the medians from the predicted FEF 25/75 values in both sexes was found in the CS group. However, no statistically significant differences were seen between the groups, which revealed a considerable scatter range for this parameter.

In Fig. 4, the FEF 75/85 values are shown. Here, ES and CS differ significantly both from NS and from PS. This, however, applies only to men.

The MEF 25/75 values show an even greater range of scatter than the prior parameters (Fig. 5). Nevertheless, here, statistically significant differentiation between the individual subgroups is possible. Thus, in the case of the men, the ES group differs from both the PS and CS, while in the women, NS and ES differ from CS.

If we compare the deviations in the predicted values of the pulmonary function parameters among the passive smoker subgroups, a heterogeneous picture is obtained. Here, FEF 25/75 (Fig. 6) and FEF 75/85 (Fig. 7) values are considered by way of example.

For the FEF 25/75 values, all the male PS groups are at about the same level (in the 100% range). By contrast, in the female PS group, a gradation is seen, with PS/W showing the smallest negative deviation from the predicted value, followed by PS/H and PS/HW (Fig. 6).

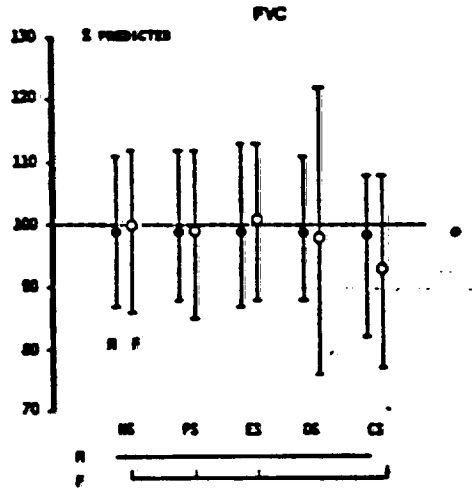

FIG. 2. Medians and 66 % confidence levels of the percentage deviations from predicted values of FVC in sex-separated subgroup comparison.

2023383721

Source: https://www.industrydocuments.ucsf.edu/docs/nryx0000

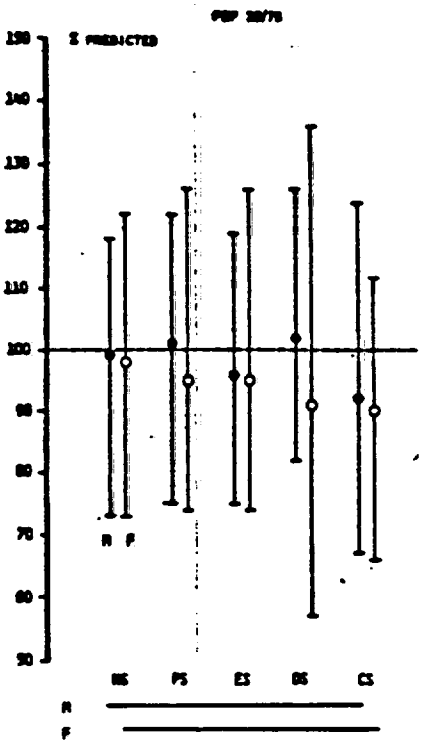

FIG. 3. Medians and 66 % confidence levels of the percentage deviations from predicted values of FEF 25/75 in sex-separated subgroup comparison.

For the FEF 75/85 measurement, the situation is almost the reverse of the FEF 25/75 medians (Fig. 7). Among the men a "ranking" can be observed in that PS/H have the best function figures, followed by PS/W and PS/HW. Among the women, the medians are scattered around the 100% range in all three groups. Neither for FEF 25/75, nor for FEF 75/85, were any statistically significant group-specific differences evident.

Dose- and Time-Effect Relationships between Tobacco Smoke Exposure and Pulmonary Function

In the CS group, the individual pulmonary function parameters were correlated with both the duration of tobacco smoke exposure and the daily consumption of cigarettes. The time-effect regressions are briefly discussed for FEF 75/85.

Among men, this parameter deteriorates with increasing duration of tobacco smoke exposure. This relationship is statistically significant at the 5% level (Fig. 8). Among women, however, no statistically significant change in FEF 75/85 as a function of the duration of exposure to tobacco smoke can be seen (Fig. 9).

For parameters FVC, FEF 25/75, and MEF 25/75, dose- and time-effect re-

2023383722

Source: https://www.industrydocuments.ucsf.edu/docs/nryx0000

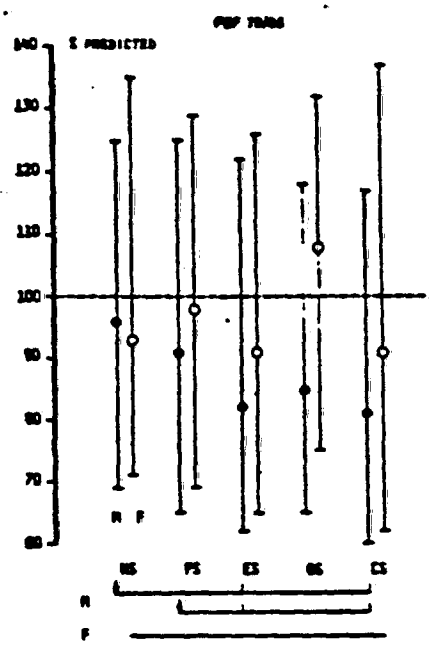

FIG. 4. Medians and 66 % confidence levels of the percentage deviations from predicted values of FEF 75/85 in sex-separated subgroup comparison.

lationships with only low correlation coefficients, not statistically significant, were observed.

DISCUSSION

Inflammation of the airways is the starting point of all chronic noncarcinogenic bronchopulmonary effects of tobacco smoke inhalation (31). Although the processes which bring about functionally significant changes following the inhalation of tobacco smoke are not yet fully known, it may be assumed that they represent multifactorial processes, for which the following pathomechanisms are under discussion:

(a) Enlargement of the mucous gland mass with resulting hypersecretion (9).

(b) Impairment of the function of the respiratory ciliated epithelium, with build-up of secretion (3).

(c) Increase in bronchial muscles (25), due to reflectory bronchoconstriction or direct bronchospasmic effects (2).

(d) Release of proteolytic enzymes from alveolar macrophages, with consecutive formation of a centro-acinar pulmonary emphysema after years of smoking (9).

(e) "Displacement" of the surfactant factor (25), with possible promotion of atelectasis.

FIG. 5.
MEF 25

The
bronch.
investi
sive ex
in the
the sm.
the pr
disease
The
things.
of vita
or flow
larger

2023383723

Source: https://www.industrydocuments.ucsf.edu/docs/nryx0000

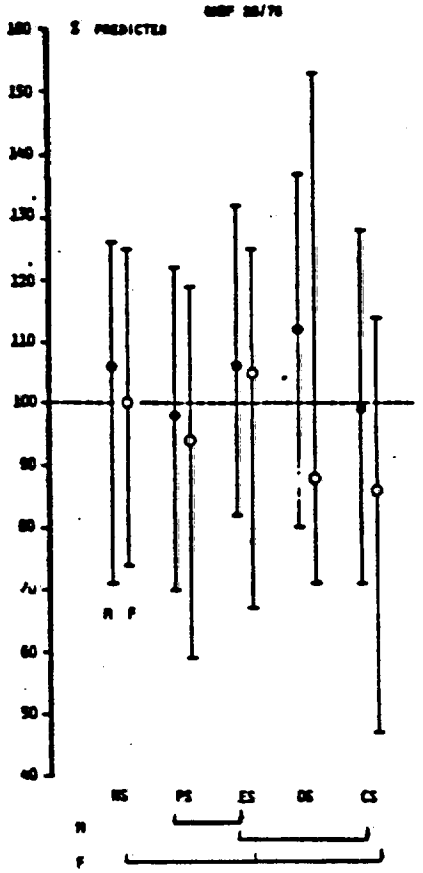

FIG. 5. Medians and 66 % confidence levels of the percentage deviations from predicted values of MEF 25/75 in the sex-separated subgroup comparison.

The inflammation of the small airways represents the initial reaction of the bronchopulmonary system to the active inhalation of tobacco smoke (9, 24). This investigation is primarily concerned with clarifying the question of whether passive exposure to tobacco smoke results in function-analytical significant changes in the small airways. There is a close correlation between structural changes of the small airways and the associated effects on pulmonary function (8), although the prognostic value of these lesions with respect to severe obstructive airway diseases has not yet been established (6, 28).

The function-analytic correlate of a small airways dysfunction is, among other things, the flow limitation in the largely effort-independent, end-expiratory part of vital capacity (20, 21, 28). This results in characteristic deformations of FVC or flow volume curves, which are relatively easy to obtain in an investigation of larger groups of subjects. Although doubts have been expressed (1, 10) on the

2023383724

Source: https://www.industrydocuments.ucsf.edu/docs/nryx0000

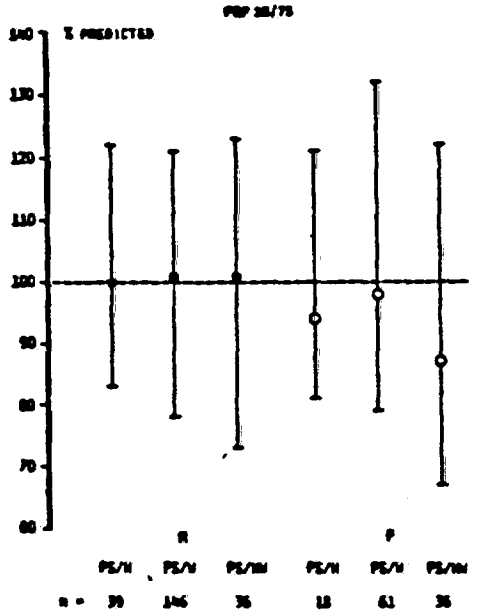

FIG. 6. Medians and 66 % confidence levels of the percentage deviations from predicted values of FEF 25/75 in the sex-separated comparison, for various types of passive smoke exposure.

specificity of such pulmonary function analyses with respect to a small airways dysfunction diagnosis, the view that the determination of parameters such as FEF 25/75, FEF 75/85, and MEF 25/75, in this respect, represents a sensible and useful function-analytic method (6, 22, 28) has largely become accepted. Admittedly, the determination of flow rates or flow differences in the diagnosis of small airways dysfunction makes sense only when normal values for such spirometric parameters as FVC and FEV, are present (10, 22, 28), that is, when significant ventilatory and respiration-mechanical disturbances affecting the large airways can be excluded. This may be assumed, for the present study, since in all subgroups, independent of sex, the FVC values scatter only in the range of a $\pm 2\%$ deviation from the predicted norm. Only the female CS group, at -7%, represents an exception. Similar remarks also apply to the FEV_1 parameter.

It is well known that end-expiratory flow determinations are subject to a large intraindividual (6) and interindividual (16) variation spectrum. For this reason, particular care was taken in this study to eliminate as far as possible, such interfering factors as prior bronchopulmonary diseases or inhaled noxae other than tobacco smoke. Furthermore, in order to limit the danger of an evaluation bias, the study was performed under blind conditions and great importance was attached to the precise standardization of the pulmonary function measuring results.

Nevertheless, it was not possible to differentiate all five subgroups defined in accordance with tobacco smoke exposure criteria, on the basis of pulmonary function analysis. It proved possible only to discriminate the CS group from all

2023383725

Source: https://www.industrydocuments.ucsf.edu/docs/nryx0000

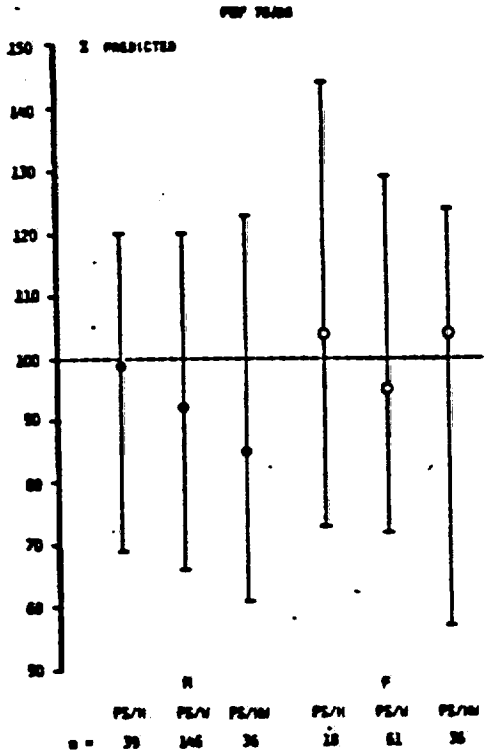

FIG. 7. Medians and 66 % confidence levels of the percentage deviations from predicted values of FEF 75/85 in the sex-separated comparison, for various types of passive smoke exposure.

categories of nonsmokers and from nonactive smokers. In this connection, FEF 75/85 and MEF 25/75 revealed the greatest discrimination. Even time- and dose-effect relationships in the CS group between tobacco smoke exposure and number of cigarettes smoked per day on the one hand, and pulmonary function on the other, revealed only a few statistically significant correlations which, however, revealed inconsistencies in the sex-separated comparison. This result is possibly due to the relatively low average age of the members of the groups investigated, particularly among women.

The precision of the measuring methodology and curve evaluation may be considered good. This was demonstrated by a parallel determination of the flow volume curve for all subjects with the aid of a second electronic spirometer which determined the measured values automatically. It may, therefore, be assumed that the heterogeneity and inconsistency of the pulmonary function pattern results mainly from the large interindividual variability of the measured data. Thus, apparent correlations may also be simulated.

On the basis of the calculations of various authors (12, 13, 15, 32), for passive smokers in general, a daily exposure of the order of magnitude of 0.2 to a max-

2023383726

Source: https://www.industrydocuments.ucsf.edu/docs/nryx0000

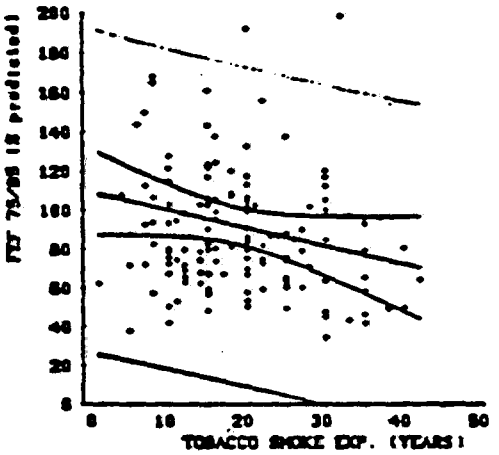

FIG. 8. Regression between FEF 75/85 and tobacco smoke exposure in years in male current smokers ($r = 0.203$, $P = 0.012$).

imum of five cigarette equivalents (depending upon the smoke constituents) may be assumed. In addition, the various types of inhalation on the part of active and passive smokers must be taken into account. While active smokers inhale primarily mainstream smoke constituents via mouth breathing, passive smokers inhale largely sidestream smoke constituents which enter the bronchial system via the nasopharynx. If additional consideration is given to the filtration function of nasal breathing, it may be stated that in the case of passive smoking one is dealing with the effects of a relatively low dose. Since, despite optimized methodology, clear and unequivocal dose- and time-effect relationships between daily cigarette consumption or smoking duration in years and pulmonary function have proved

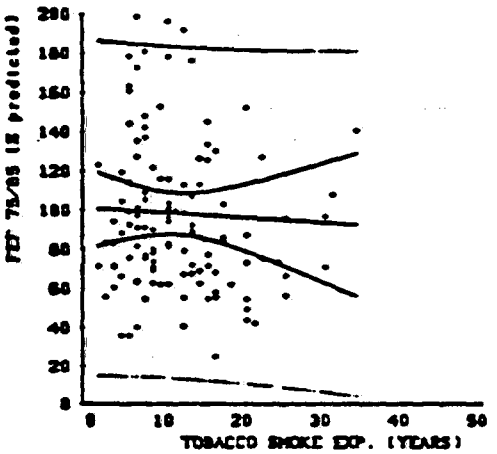

FIG. 9. Regression between FEF 75/85 and tobacco smoke exposure in years in female current smokers ($r = 0.042$, $P = 0.641$).

2023383727

Source: https://www.industrydocuments.ucsf.edu/docs/nryx0000

impossible to establish or have been established only in an inconsistent form (as in the case of CS), this is all the more likely to be the case for the low-dose situation met with in passive smoking.

As mentioned at the beginning of this article, only a few studies have so far considered the question of possible impairment of pulmonary function in adult passive smokers. These studies all have the disadvantage, owing to the nature of the data collection, of not being able to form groups for all possible factors of active and passive tobacco smoke exposure. This means that there is a danger of selection bias involving the nonconsideration of possible positive or negative results. Since, however, a similar pulmonary function methodology was employed, comparisons between our results and those reported in other studies are possible.

In common with us, Schilling *et al.* (27) and Comstock *et al.* (7) were unable to establish any statistically significant reduction of pulmonary function in passive smokers (Table 4). In contrast, Kauffmann *et al.* (14) found differences between

TABLE 4

REVIEW OF THE LITERATURE ON ARTICLES SO FAR PUBLISHED ON THE TOPIC PULMONARY FUNCTION IN PASSIVE SMOKERS

Authors	Subgroups*		Pulmonary function parameter	Results*
Schilling *et al.*, 1977	NS/H PS/H CS	N = 138 114 78	FVC, FEV_1 PEF, MEF 50 MEF 25	No statistically significant reduction of lung function for PS/H.
White and Frueh, 1980	NS PS/W CS	N = 400 400 1300	FVC, FEV_1 FEF 25/75	Concerning FEF 25/75 and FEF 75/85: PS/W show statistically significantly lower values than NS. Values in PS/W do not differ essentially from values in CS smoking 1–10 cigarettes per day and in CS without inhalation.
Comstock	PS/H ES/H CS	N = 539 232 953	FEV_1 FEV_1/FVC	No statistically significant reduction of lung function for PS/H.
Kauffmann	NS/H PS/H	N = 1675 1223	FVC, FEV_1 FEF 25/75	Concerning FEF 25/75 in females aged 40 years or more: statistically significant differences between NS and PS/H. Dose–effect relationship between reduction of lung function in PS/H and daily tobacco consumption of the husband.

* See text for abbreviations.

2023383728

Source: https://www.industrydocuments.ucsf.edu/docs/nryx0000

never smokers and passive smokers at home with regard to the FEF 25/75 parameter, and also a dose–effect relationship between the reduction in pulmonary function in passive smokers and the daily tobacco consumption of the subject's spouse. However, these relationships were statistically significant only for women, and then only for certain age groups. To date, White and Froeb (35) are the only authors who unreservedly find that passive smoking leads to an impairment of pulmonary function. The predicted value reductions in the case of persons passively exposed to tobacco smoke at the workplace do not, however, differ essentially from those seen in active smokers consuming between 1 and 10 cigarettes a day. This result is difficult to reconcile with a rational dose–effect relationship under the assumptions made earlier [see also Lebowitz (19)].

Taking our own results into consideration, it seems that the passive inhalation of tobacco smoke at home or in the workplace by healthy individuals probably does not lead to any essential impairment of pulmonary function. To what extent this also applies to extreme passive exposure to smoke must remain the subject of further investigation. Thus, for example, persons working in restaurants or in poorly ventilated rooms may be exposed to high levels of smoke pollution.

ACKNOWLEDGMENTS

We thank Dr. Mentzel, Bundesanstalt für Arbeit, Nuremberg; Dr. Jahn, from the firm of Diehl, Nuremberg; Dr. Bressel and Dr. Heynen from the firm of Siemens, Erlangen, Medical Engineering Group, and the management of the various firms, the personnel directors, and the employee representatives who supported our investigation and made the study possible. Further, we express our special thanks to Mrs. Schmidt and Mrs. Weydanz for carrying out the pulmonary function analyses and establishing the data records.

REFERENCES

1. Bake, B. Is maximum mid-expiratory flow rate sensitive to small airways obstruction? *Eur. J. Respir. Dis.* 62, 150–151 (1981).
2. Berend, N., Wright, J. L., Thurlbeck, W. M., Martin, G. E., and Woolcock, A. J. Small airways disease: Reproducibility of measurement and correlation with lung function. *Chest* 79, 263–268 (1981).
3. Camner, P., Philipson, K., and Arvidsson, T. Withdrawal of cigarette smoking: A study on tracheobronchial clearance. *Arch. Environ. Health* 26, 90–92 (1973).
4. Cherniack, R. M., and Raber, M. B. Normal standards for ventilatory function using an automated wedge spirometer. *Amer. Rev. Respir. Dis.* 106, 38–46 (1972).
5. Dodge, R. The effects of indoor pollution on Arizona children. *Arch. Environ. Health* 37, 151–155 (1982).
6. Cochrane, G. M., Prieto, F., and Clark, T. J. H. Intrasubject variability of maximal expiratory flow volume curve. *Thorax* 32, 171–176 (1977).
7. Comstock, G. W., Meyer, M. B., Helsing, K. J., and Tockman, M. S. Respiratory effects of household exposures to tobacco smoke and gas cooking. *Amer. Rev. Respir. Dis.* 124, 143–148 (1981).
8. Cosio, M. H., Ghezzo, H., Hogg, J. C., Corbin, R., Loveland, M., Dosman, J., and Macklem, P. T. The relation between structural changes in small airways and pulmonary function tests. *New Engl. J. Med.* 298, 1277–1281 (1977).
9. Cosio, M. G., Hale, K. A., Niewoehner, D. E. Morphologic and morphometric effects of prolonged cigarette smoking on the small airways. *Amer. Rev. Respir. Dis.* 122, 265–271 (1980).
10. Gelb, A. F., Williams, A. J., and Zamel, N. Spirometry—FEV_1 vs FEF 25–75 Percent. *Chest* 84, 473–747 (1983).
11. Hasselblatt, U., Humble, C. G., Graham, M. G., and Anderson, H. S. Indoor environmental determinants of lung function in children. *Amer. Rev. Respir. Dis.* 123, 479–85 (1981).

2023383729

Source: https://www.industrydocuments.ucsf.edu/docs/nryx0000

12. Hegud, C., Hawkins, L. H., and Astrup, P. Exposure of passive smokers to tobacco smoke constituents. *Int. Arch. Occup. Environ. Health* 42, 21–29 (1978).
13. Hegud, C. Indoor air pollution with smoke constituents—An experimental investigation. *Prev. Med.* 13, 582–588 (1984).
14. Kauffmann, F., Tessier, J. F., and Oriol, P. Adult passive smoking in the home environment: A risk factor for chronic airflow limitation. *Amer. J. Epidiol.* 117, 269–280 (1983).
15. Klosterkötter, W., and Gono, E. Zum Problem des Passivrauchens. *Zentralbl. Bakteriol. Hyg. I. Abt. Orig. B* 162, 51–69 (1976).
16. Knudson, R. J., Burrows, B., and Lebowitz, M. D. The maximal expiratory flow-volume curve: Its use in the detection of ventilatory abnormalities in a population study. *Amer. Rev. Respir. Dis.* 114, 871–879 (1976).
17. Knudson, R. J., Slatin, R. C., Lebowitz, M. D., Burrow, B. The maximal expiratory flow-volume curve. Normal standards, variability and effects of age. *Amer. Rev. Respir. Dis.* 113, 587–600 (1976).
18. Lebowitz, M. D., Armet, D. B., and Knudson, R. The effect of passive smoking on pulmonary function in children. *Environ. Internat.* 8, 371–373 (1982).
19. Lebowitz, M. D. "Influence of Passive Smoking on the Pulmonary Function—A Survey." Unpublished data.
20. McFadden, E. R., and Linden, D. A. A reduction in maximum mid-expiratory flow rate. *Amer. J. Med.* 52, 725–737 (1972).
21. McFadden, E. R., Kiker, R., Holmes, B., and Degroot, W. J. Small airway disease. *Amer. J. Med.* 57, 171–182 (1974).
22. McFadden, E. R., and Ingram, R. H. Peripheral airway obstruction. *J. Amer. Med. Assoc.* 235, 259–260 (1976).
23. Morris, J. F., Koski, A., and Johnson, L. C. Spirometric standards for healthy nonsmoking adults. *Amer. Rev. Respir. Dis.* 103, 57–67 (1971).
24. Niewoehner, D. E., Kleinerman, J., and Rice, D. B. Pathologic changes in the peripheral airways of young cigarette smokers. *New Engl. J. Med.* 10, 755–758 (1974).
25. Petty, T. L., Silvers, G. W., Stanford, R. E., Baird, M. A., and Mitchell, R. S. Small airway pathology is related to increased closing capacity and abnormal slope of Phase III in excised human lungs. *Amer. Rev. Respir. Dis.* 121, 449–456 (1980).
26. Quanjer, P. H., (Ed.). "Standardized Lung Function Testing." European Community for Coal and Steel, Luxembourg, July 1983.
27. Schilling, R. S. F., Letai, A. D., Hui, S. L., Beck, G. J., Schoenberg, J. B., and Bouhuys, A. Lung function, respiratory disease and smoking in families. *Amer. J. Epidemiol.* 106, 274–283 (1977).
28. Schulz, V. Small airways disease. *Prax. Pneumol.* 34, 187–218 (1980).
29. Speizer, F. E., Ferris, B. J., Bishop, Y. M. M., and Spengler, J. Respiratory disease rates and pulmonary function in children associated with NO_2 exposure. *Amer. Rev. Respir. Dis.* 121, 3–10 (1980).
30. Tager, I. B., Weiss, S. T., Rosner, B., and Speizer, F. E. Effect of parental cigarette smoking on the pulmonary function of children. *Amer. J. Epidemiol.* 110, 15–26 (1979).
31. Thurlbeck, W. M. Smoking, airflow limitation, and the pulmonary circulation. *Amer. Rev. Respir. Dis.* 122, 183–186 (1980).
32. Vutuc, C. Lungenkrebsrisiko und Passivrauchen: Quantitative Überlegungen. *Zentralbl. Bakteriol. Hyg. I. Abt. Orig. B* 177, 90–95 (1983).
33. Weiss, S. T., Tager, I. B., Speizer, F. E., and Rosner, B. Persistent wheeze: Its relationship to respiratory illness, cigarette smoking and level of pulmonary function in a population sample of children. *Amer. Rev. Respir. Dis.* 122, 697–707 (1980).
34. Weiss, S. T., Tager, I. B., Schenker, M., and Speizer, E. The health effects of involuntary smoking. *Amer. Rev. Respir. Dis.* 128, 933–942 (1983).
35. White, J. R., and Frueb, H. F. Small-airways dysfunction in nonsmokers chronically exposed to tobacco smoke. *New Engl. J. Med.* 302, 720–723 (1980).
36. Kruskal, W. H., and Wallis, W. A. Use of ranks in one-criterion variance analysis. *J. Amer. Statist. Ass.* 47, 583–627 (1952).

2023383230

Source: https://www.industrydocuments.ucsf.edu/docs/nryx0000